From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

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PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL PRELIMINARY EXAMINATION REPORT
(PCT Rule 71.1)

Date of mailing *(day/month/year)*	25.10.2001
Applicant's or agent's file reference: 11041-98	**IMPORTANT NOTIFICATION**

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/CA00/00777	28/06/2000	28/06/1999

Applicant
NATIONAL RESEARCH COUNCIL OF CANADA et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/	Authorized officer
European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Hingel, W Tel.+49 89 2399-8717

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
11041-98		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/CA00/00777	28/06/2000	28/06/1999
International Patent Classification (IPC) or national classification and IPC C12N9/00		
Applicant NATIONAL RESEARCH COUNCIL OF CANADA et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 8 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   - VI ☒ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
24/01/2001	25.10.2001
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Barnas, C Telephone No. +49 89 2399 7469

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/CA00/00777

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:
Description, pages:

1-45 as originally filed

Claims, No.:

1-70 as originally filed

Drawings, sheets:

1-5 as originally filed

Sequence listing part of the description, pages:

1-13, as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☒ contained in the international application in written form.
- ☒ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

   ☐ the entire international application.

   ☒ claims Nos. 3, 7-12, 17, 21-26, 31, 35-40, 44, 48, 61, 69 (all completely); 1, 13-15, 27-29, 41, 42, 45, 46, 49-59, 62-67, 70 (all partially).

because:

- ☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):

- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

- ☒ no international search report has been established for the said claims Nos. 3, 7-12, 17, 21-26, 31, 35-40, 44, 48, 61, 69 (all completely); 1, 13-15, 27-29, 41, 42, 45, 46, 49-59, 62-67, 70 (all partially).

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

   ☐ the written form has not been furnished or does not comply with the standard.

   ☐ the computer readable form has not been furnished or does not comply with the standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	27, 62, 64, 65
	No:	Claims	1, 2, 4-6, 13-16, 18-20, 28-30, 32-34, 41-43, 45-47, 49-60, 63, 66-68, 70
Inventive step (IS)	Yes:	Claims	62
	No:	Claims	27, 49-52, 54-58, 64, 65
Industrial applicability (IA)	Yes:	Claims	1-70
	No:	Claims	

2. Citations and explanations
see separate sheet

VI. Certain documents cited

1. Certain published documents (Rule 70.10)

and / or

2. Non-written disclosures (Rule 70.9)

see separate sheet

Re Item I

Basis of the opinion

The examination has been restricted to the Helicobacter galactosyltransferase (see ISR).

It was not possible for the IPEA to check whether the subsequently-filed sequence listing (received 27.7.2000) constitutes added matter. Examination has therefore been carried out on the basis of the sequences or sequence listing as filed.

Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

D1: TOMB J -F ET AL: 'THE COMPLETE GENOME SEQUENCE OF THE GASTRIC PATHOGEN HELICOBACTER PYLORI' NATURE,GB,MACMILLAN JOURNALS LTD. LONDON, vol. 388, no. 6642, 7 August 1997 (1997-08-07), pages 539-547,TABEL, XP002062106 ISSN: 0028-0836 cited in the application -& DATABASE EMBL [Online] Accession AE000594, 25 August 1997 (1997-08-25) TOMB J -F ET AL: 'Helicobacter pylori 26695 section 72 of 134 of the complete genome.' XP002155934

D2: WO 96 40893 A (ASTRA AB ;BERGLINDH O THOMAS (SE); MELLGAERD BJOERN L (SE); SMITH) 19 December 1996 (1996-12-19)

D3: WANG G ET AL: 'MOLECULAR GENETIC BASIS FOR THE VARIABLE EXPRESSION OF LEWIS Y ANTIGEN IN HELICOBACTER PYLORI: ANALYSIS OF THE ALPHA(1,2) FUCOSYLTRANSFERASE GENE' MOLECULAR MICROBIOLOGY,GB,BLACKWELL SCIENTIFIC, OXFORD, vol. 31, no. 4, February 1999 (1999-02), pages 1265-1274, XP000889904 ISSN: 0950-382X

D4: CHAN N W ET AL: 'THE BIOSYNTHESIS OF LEWIS X IN HELICOBACTER PYLORI' GLYCOBIOLOGY,GB,IRL PRESS,, vol. 5, no. 7, 1995, pages 683-688, XP002920175 ISSN: 0959-6658 cited in the application

1. Art. 33(2) PCT, Novelty

1.1. D1 ISR discloses an isolated recombinant polynucleotide containing the coding region (nucleotides 1551-2372) for the Helicobacter pylori β-1,4-galactosyltransferase (HP0826 see Table 2, "Cell Envelope Genes", right column). Said coding region shows 100% identity to SEQ ID NO: 1. Because this polynucleotide comprises nucleotides located 5' to the coding region it is expected to contain of the 1,4-galactosyltransferase promoter. D1

is, therefore novelty destroying for **claims 1, 2, 4-6, 13, 14, 29, 30, 32-34, 41-43 and 45.**

1.2. D2 discloses an isolated H. pylori polypeptide with the amino acid sequence SEQ ID NO. 1887. Said polypeptide shows 94.8% identity in a 273 amino acid overlap to the amino acid sequence SEQ ID NOs: 2 of the H. pylori β-1,4-galactosyltransferase of the specification. Because of the high sequence homology, said isolated polypeptide of D2 is regarded as β-1,4-galactosyltransferase. D2 (p. 33, ln. 8-11 and ln. 25-30) further discloses host cells which comprise a vector with an expression cassette containing the nucleic acid encoding said polypeptide. D2 also describes a method to produce said polypeptide using said host cell. D2 is therefore, novelty destroying for **claims 15, 16, 18-20, 28, 46, 47, and 53.**

1.3. D3 (p. 1268, right column) discloses a mutant H.pylori strain having deactivated the α(1,2) fucosyltransferase gene. **Claims 59, 60 and 66** are, therefore, not new.

1.4. Claims 63 embraces vaccines comprising any antigen including any immunogenic protein from the mutant H. pylori strain of claim 59. Such immunogenic proteins derived from the mutant strain, however, cannot, be distinguished from a wild type strain. Thus **claim 63** embraces vaccines which cannot be distinguished from known vaccines (see eg. D2) and is, therefore, not new.

1.5. D4 (p. 686, right column, second paragraph "Activity screening") discloses a reaction mixture suitable for an enzymatic synthesis of a Helicobacter lipopolysaccharide and of a mimic of a Helicobacter lipopolysaccharide. Said disclosure is novelty destroying for **claims 67, 68 and 70.**

1.6. Claims 1, 15, 27, 29, 42, 46 and **49-58** describe "a portion" or "fragments" of a nucleic acid or a polypeptide. Said wording embraces any fragment including fragments consisting of only one nucleotide or one amino acid. Said claims and claims dependent thereon are, therefore, also because of this reason not new.

2. Art. 33(3) PCT, Inv ntiv Step

2.1. The isolation of a polypeptide which is encoded by a known nuclei acid represents a routine method which the skilled person would apply and does not comprise an inventive

step. The β-1,4-galactosyltransferase with the amino acid sequence SEQ ID NO: 2 (claim 27) encoded by the known SEQ ID NO: 1 is, therefore, not inventive.

2.2. D3 (p. 686, left column, last paragraph, ln. 5-11) describes β-1,4-galactosyltransferase activities in H. pylori. Said document states that there are different strains of H. pylori which differ at the genome level. D3 teaches further the isolation of homogenous enzymes and sequencing and cloning of the galactosyltransferases. The isolation of the β-1,4-galactosyltransferases with the amino acid sequences SEQ ID NOs: 2 and 10 and their coding nucleic acids SEQ ID NOs: 1 and 9 follows, therefore, the teaching of D3 and is not inventive. **Claim 27** is, therefore, not inventive.

2.3. Claims 64 and 65 are directed to vaccines containing a mutant lipopolysaccharide. The specification, however, does not shown any specific effect resulting from such vaccines. Thus, said vaccines are regarded as arbitrary modifications of known vaccines comprising wild-type lipopolysaccharides (see e.g. D2) and **claims 64 and 65** are, therefore, not inventive.

2.4. **Claims 49-52 and 54-58** relate to subject matter which the skilled person would provide, according to the circumstances, by applying standard methods without the use of inventive skill. Said claims are, therefore, not inventive.

3. Additional Observations

A mutant H. pylori strain having deactivated a glycosyltransferase coded by the open reading frames indicated in claim 62 cannot be derived from the cited prior art in an obvious manner. Claim 62 is, therefore, inventive.

Re Item VI

Certain documents cited, Certain published documents (Rule 70.10)

Application No Patent No	Publication date *(day/month/year)*	Filing date *(day/month/year)*	Priority date *(valid claim)* *(day/month/year)*
WO99/40205	12.8.99	27.1.99	4.2.98

The above listed document was published after but filed before the priority date of the

present application. It does, therefore, not belong to the state of the art according to Rule 64(1)(b) PCT. It will, however, become of relevance for the novelty of the claimed subject matter during regional phase examination, and if it later turns out that the priority of the present application has not been correctly claimed, also for the inventive step involved with the claimed subject matter.